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Lifestyle factors, hormonal contraceptives and premenstrual symptoms: The UK Southampton Women's Survey

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Abstract

Objective—To estimate the prevalence of premenstrual symptoms in women from the general population in Southampton, UK, and examine their association with lifestyle factors and contraceptive usage.

Design—Cross-sectional survey.

Setting—The City of Southampton, UK.

Population—974 women aged 20-34 years (53% of the 1,841 women invited to participate).

Methods—Interviews, questionnaires and completion of a prospective six-week menstrual symptom diary recording on a daily basis the presence and severity of eleven common premenstrual symptoms.

Main outcome measures—Premenstrual symptoms were identified from the diaries by two clinicians who reviewed them independently using a pre-defined algorithm to assess the onset and decline of symptoms in relation to the start of menstruation.

Results—24% of the women were considered to have premenstrual symptoms (95% confidence interval [CI] 21% to 27%). Women were less likely to have symptoms if they had higher levels of educational attainment and suffered less from stress. No associations were found between premenstrual symptoms and diet, alcohol or strenuous exercise, nor after adjustment for other factors, with age, smoking or body mass index. Use of any form of hormonal contraceptives **was associated with a lower prevalence of** premenstrual symptoms (prevalence ratio 0.66 (95%CI: 0.52 to 0.84)).

Conclusions—Premenstrual symptoms were common in this cohort. Use of hormonal contraceptive methods was associated with a lower prevalence of these symptoms.

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Introduction

Data from the US 2002 National Health Interview Survey indicate that 19% of young women have premenstrual syndrome (PMS) or other menstrual-related problems[1]. Women with PMS often report cyclical symptoms that can either be psychological, such as irritability, or physical, such as headaches and back pain[2]. These conditions can impact on quality of life[3], affecting relationships both at work and home[2].

Premenstrual symptoms have been linked to anxiety and depression[1] and are associated both with direct medical costs as well as indirect costs due to absenteeism and low productivity in the workplace[3,4]. There may be substantial public health implications, as women with premenstrual symptoms are more likely to smoke tobacco, drink alcohol and be overweight[1].

The etiology of premenstrual symptoms is uncertain. An interaction between the neuroendocrine system and a woman's sensitivity to the changes in plasma levels of steroid hormones such as estradiol and progesterone are thought to be important[5]. A wide range of different treatment regimes including lifestyle, complementary and drug therapies have been advocated for the specific disorders of premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD)[6-8]. Examples of complementary therapies include Vitamin B6[9] and cognitive behavior therapy[10]. Selective serotonin reuptake inhibitors have been shown to be effective given both continuously and cyclically[11,12]. Cyclical progesterone therapy has been advocated[13] but multiple trials and meta-analyses have shown progesterone to be ineffective[14,15], although these studies mainly looked at cyclical use of progesterone rather than continuous use. Estrogen, delivered either as patches or implants has been shown in several studies to help PMS[16,17]. In addition, recent studies have shown a positive outcome with combined oral contraceptives containing drospirenone given either cyclically or as a 168 day extended regime[18-20].

The Southampton Women's Survey[21] (SWS) is a study of 12,500 young women primarily aimed at unraveling the determinants of the growth and development of their children. Data have been collected on factors such as employment, socio-demographic status, age, ethnicity, physical activity and diet. In this sub-study we have used a menstrual symptom diary in an attempt to identify women within this cohort who have premenstrual symptoms, and then to search for associations with lifestyle factors and contraceptive use.

Materials and Methods

Participants in the SWS were recruited via their General Practitioners (GPs), a profession equivalent to family doctors in the US. A home visit by a research nurse allowed us to obtain data on sociodemographic status, lifestyle, body composition, educational qualifications, ethnicity and diet. We also obtained detailed information on contraceptive use. Following this initial interview, women were invited to provide a blood sample for measurement of a number of parameters for the main study. In October 2001, towards the end of the blood-sampling phase, the premenstrual symptoms sub-study was started. All 1,841 women attending from then until the end of the phase in February 2003, were asked whether they would be interested in taking part in this sub-study. These participants were asked to complete a six-week menstrual symptom diary (a modified version of the validated Moos Menstrual Distress Questionnaire[22]) in addition to the standard interviews and questionnaires.

Educational grades in the UK are not easily converted to their USA equivalents. We used five categories of qualifications ranging from category 1 (approximating Grade School), category 3 (High School Diploma) and category 5 (Bachelor's Degree or above). Diet in the

SWS was assessed using a 100-item food frequency questionnaire, previously analyzed using principal components analysis[23]. The first principal component can be interpreted as a summary of the degree to which each woman follows healthy eating recommendations. This has been termed the 'prudent diet score' and is used here to assess associations between premenstrual symptoms and a healthy diet.

The menstrual questionnaire recorded the presence and severity of 11 common premenstrual symptoms: irritability, loss of efficiency, difficulty concentrating, tiredness, mood swings, tension, depression, headaches, food craving, acne and fluid retention (breast tenderness, weight gain or swollen/bloated). Two GPs (CS and RB) independently assessed these diaries using criteria developed following a review of definitions of the premenstrual syndrome and premenstrual dysphoric disorder[2,24].

Our definition of premenstrual symptoms was made according to the following criteria:

1. a pattern of symptoms occurring in the days leading up to menstruation that resolved completely or greatly improved by the end of menstruation,
2. an interval of ≥ 7 days before symptoms recurred, and
3. ≥ 5 symptoms scored as mild or moderate or ≥ 2 symptoms scored as severe, with each symptom following the pattern described above.

The two GPs independently scored each diary as: 1 (no premenstrual symptoms), 2 (possible symptoms) or 3 (definite symptoms). Where one scored 3 and the other scored 1, the diary was reviewed independently by both GPs and their scores revised if appropriate. In cases of continued disagreement, the GPs met with an arbitrator (HI) to decide on the final score. The scores from the two GPs were added together giving total scores ranging from 2 to 6. Women with scores of 5 or 6 were classified as having premenstrual symptoms, while women with scores equal to or less than 4 were classified as having insufficient symptoms to meet the case definition. As our method does not consider women over a number of cycles and we have no information on the effect of symptoms on daily living, our definition does not conform to formal definitions of premenstrual syndrome[7,8,25] and hence our use of the term 'premenstrual symptoms'.

The data analysis was performed by examining the differences between women with and without premenstrual symptoms. Tabulations and Student's *t*-tests were used to explore categorical and continuous variables respectively. Prevalence ratios were calculated using a generalized linear model with a log link and a binomial error structure (binomial regression)[26]. When the prevalence of the outcome is common, odds ratios derived from a logistic regression cannot be interpreted as approximations to prevalence ratios; this modeling approach provides direct estimates of prevalence ratios. The risk factors identified *a priori* as possibly linked to premenstrual symptoms were age, educational attainment, smoking status, alcohol consumption, body mass index (BMI), contraceptive use, taking strenuous exercise, reported level of stress, and the type of diet consumed. These data were explored initially in a univariate analysis. Subsequently we developed a multiple regression model by adding variables in a forward step-wise way according to the level of significance in preceding models. The process was considered complete when no further variables could be added such that they made a significant contribution to the model at the 5% level.

Results

Of the 1,841 women asked to participate in this study, 974 (53%) returned a menstrual symptom diary, of which 44 were incomplete and one was found to be outside the age range for the study. Analysis of the diaries led to identification of premenstrual symptoms in 224

women (24%, 95% confidence interval [CI] 21 to 27%). These women had a mean GP coding score of 5.6 compared to a mean score of 2.1 for the remaining women who were classified as having no premenstrual symptoms. If none of the 912 women who did not return a complete diary had met the criteria then the prevalence of premenstrual symptoms in this cohort would have been 12%. We compared the characteristics of responders to the full SWS study population (Table 1) to look for non-response bias, as women with premenstrual symptoms may be more likely to participate than non-sufferers. Participants in this sub-study tended to be somewhat older and better educated than the full study population but the degree of perceived stress was similar. Slightly more of the responders were hormonal contraceptive users, but the proportions taking progestins were similar. Such differences might have a small impact on our overall assessment of prevalence of premenstrual symptoms but should not unduly affect the internal comparisons examining the risk factors. **For the risk factor analyses we have excluded a further 71 women who had no discernable menstrual cycle.**

In univariate analyses, women with premenstrual symptoms tended to be older, have a lower level of educational achievement, were more likely to smoke, have a higher body mass index (BMI), and a higher perceived level of stress (Table 2). There was no significant difference between those with premenstrual symptoms and those without symptoms with respect to their ‘prudent diet score’, alcohol intake or level of strenuous exercise (data not shown).

Premenstrual symptoms were substantially less common in those women currently using hormonal contraceptives (prevalence ratio 0.63, 95% CI 0.50 to 0.81) (Table 2). Compared with those not using any form of hormonal contraception, symptoms were less common in those using noninjectable progestin-only methods, such as the progestin-only pill, the progestin implant etonogestrel, and the levonorgestrel-releasing intrauterine system (prevalence ratio 0.54, 95% CI 0.26 to 1.14), and in those using combined (estrogen-progestin) oral contraceptives (prevalence ratio 0.66, 95% CI 0.52 to 0.84). Premenstrual symptoms were not identified in any of the nine women using injectable progestins such as medroxyprogesterone acetate and norethisterone enantate with prevalence ratio 0.0 ([upper] 95% confidence point 1.11).

In a multiple regression model, use of hormonal contraceptives, perceived level of stress, and educational qualifications remained statistically significant (Table 2), but smoking, BMI, and age were no longer related to premenstrual symptoms.

In terms of alternative progestins in combined oral contraceptives, only one woman was taking drospirenone/ethinylestradiol as it was not launched in the UK until 2002 and the low estrogen-dose variant of drospirenone/ethinylestradiol is not yet in use in the UK.

Discussion

Main findings

We have shown that premenstrual symptoms occur commonly in the Southampton Women’s Survey cohort (12 - 24% of women aged 20 - 34 years) and these symptoms were linked to various lifestyle and other factors. In particular high stress, and lower educational qualifications were associated with increased prevalence of premenstrual symptoms, while the prevalence was lower in those who used hormonal contraception . Premenstrual symptoms were more common in those who were older, more obese (also reported by Strine[1] and Hourani[27]) or who smoked tobacco (also demonstrated by Strine[1] and Kritz-Silverstein[28]), but such associations were lost when adjusted for contraceptive usage,

possibly reflecting prescribing practice, such that certain women, for example those who are obese, may be less likely to be prescribed particular contraceptives.

Comparison with other studies

The associations between premenstrual symptoms, a high perceived level of stress and a low level of educational achievement have been reported elsewhere[1,27]. Hourani *et al*[27] specifically focused on job stress in military women but our more general measure of stress, similar to those used elsewhere[1] identifies stress in any area of life as being associated with premenstrual symptoms. Our lack of an association between diet (measured using the 'prudent diet score') and premenstrual symptoms is consistent with the overall findings of the recent Study of Women's Health Across the Nation (SWAN), a survey of 3,302 midlife US women[29]. This latter study found some links between certain PMS symptoms and alcohol consumption, in common with other studies[1,27], though, we did not find an association between premenstrual symptoms and alcohol use in our study.

The associations we have described with hormonal contraceptives are intriguing as they are derived from a large community-based cohort. Some authors argue that contraceptives have a place in the treatment of PMS[30]. Notably, three recent studies reported the benefit of drospirenone-containing combined oral contraceptives in alleviating symptoms of premenstrual dysphoric disorder either on a 168 extended regime[18] or cyclically with a shorter hormone-free interval than the usual seven days per cycle.[19,20,30]. In the case of injectable progestins it must be noted that there have been no formal controlled trials of their ability to prevent PMS. However, a recent survey of 6,026 US military women[27] reported a strikingly low prevalence of premenstrual symptoms in users of injectable progestins (odds ratio 0.18, 95% CI 0.10 to 0.32), consistent with our own findings.

Strengths and weaknesses

This was a study of women from the general population, rather than those reporting to clinics or hospitals with symptoms. While diagnostic criteria have been developed for specific disorders such as premenstrual syndrome (PMS)[7,8,25] and premenstrual dysphoric disorder (PMDD)[24], these focus on diagnosis in a clinical setting and require diaries to be kept over a number of cycles. This is a challenge in general population research where many women do not suffer from symptoms and are less motivated to complete diaries over a long time period, thus biasing the results. We considered that six weeks was the longest time period for which we could ask women to record symptoms without severely affecting our response rate. A recent general population study over two menstrual cycles reported a similar return rate of completed diaries as in our study[31]. We also were unable to assess the effect of symptoms on daily living and some women may have been suffering from premenstrual symptoms that were an exacerbation of another disorder, but the diaries could not identify this robustly. Thus we do not claim to have assessed PMS according to current definitions[7,8,25], and so have described the condition simply as premenstrual symptoms throughout.

We studied women from the general population and assessed associations with prevalence of the symptoms rather than the effect of therapy. Further confounders may be operating in a number of ways; for example, the need for contraception could indicate a healthier, more socially engaged population of women who are sexually active and less prone to debilitating symptoms. However, the symptoms were common in our population and although affecting quality of life for a few days each month would be unlikely to prevent the women from leading generally active lives.

Interpretation and implications

To date the therapeutic trials of hormone treatments for PMS, rather than PMDD as discussed above, have proved inconclusive[14,15,32], but this may be because they assessed cyclical rather than continuous regimes. Observational evidence from our work and elsewhere[18,27,30,33] suggests that hormonal contraceptive methods that suppress ovulation and act continuously may have a role in preventing premenstrual symptoms. This provides some support in favor of large well-powered randomized controlled trials of methods that induce amenorrhea in the treatment of premenstrual symptoms.

Conclusions

Premenstrual symptoms were common in this cohort of women and occurred more frequently in those with lower levels of educational attainment and in those who reported having suffered more from stress. All forms of hormonal contraception were associated with a lower prevalence of symptoms. The possible protective action of contraceptive methods that induce amenorrhea and act continuously deserve further study.

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Table 1

Characteristics of the women who completed the menstrual symptom diaries compared with the entire Southampton Women's Survey cohort.

Characteristic	Those completing menstrual diaries	Entire SWS cohort[1]
Age (years)		
<25	142 (15.3%)	3,333 (26.6%)
25-29	309 (33.3%)	4,319 (34.4%)
30-34	478 (51.5%)	4,899 (39.0%)
Age at initial interview in years [mean (SD)]	29.6 (3.8)	28.2 (4.2)
Highest educational attainment[2] n (%)		
I (lowest level)	106 (11.5%)	2,107 (16.9%)
2	228 (24.8%)	3,313 (26.5%)
3	320 (34.7%)	3,729 (29.9%)
4	54 (5.9%)	724 (5.8%)
5 (highest level)	213 (23.1%)	2,613 (20.9%)
Number currently smoking (%)	174 (18.8%)	3,858 (30.8%)
BMI kg/m^2 [median (interquartile range)]	24.5 (22.3-27.7)	24.1 (21.8-27.5)
Reported extent to which stress has affected life		
None	229 (24.7%)	2,841 (22.7%)
Slightly	357 (38.4%)	4,721 (37.7%)
Moderately	183 (19.7%)	2,357 (18.8%)
Quite a lot	135 (14.5%)	2,131 (17.0%)
Extremely	25 (2.7%)	468 (3.7%)
Contraceptive type [3]		
None	443 (49.1%)	3,096 (51.6%)
Combined OC	379 (42.0%)	2,359 (39.3%)
Progestin-only pill, **etonogestrel, levonorgestrel**	47 (5.2%)	291 (4.9%)
Injectable progestins	34 (3.8%)	257 (4.3%)
White ethnic group	907 (97.7%)	11,785 (94.1%)
In receipt of social security benefits	128 (13.8%)	2,204 (17.6%)

[1] Frequencies do not necessarily sum to the same totals due to missing data.

[2] Educational levels are explained in the methods section of the paper.

[3] Data on contraceptive type was not requested from the women in the earlier part of the SWS, so these data are only available for 6003 women.

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Table 2

Prevalence of premenstrual symptoms in relation to lifestyle factors in the Southampton Women's Survey. Variables are listed where univariate analysis showed a significant association with premenstrual symptoms at the 5% level of significance. Total numbers studied for each risk factor vary due to missing data. 71 women with no discernable menstrual cycle have been excluded from the analysis.

Variable	Number studied	Number and prevalence (%) of premenstrual symptoms	Prevalence ratio (95% CI) (univariate analysis)	Prevalence ratio (95%CI) (final multivariate model)
Age group (y)				
<25	133	22 (17%)	**1** (baseline)	
25-29	287	78 (27%)	**1.64** (1.07 to 2.52)	
30-34	438	124 (28%)	**1.71** (1.14 to 2.58)	
			$P_{trend} = 0.02$	
Educational qualifications				
I (lowest level)	98	33 (34%)	**1** (baseline)	**1** (baseline)
2	205	59 (29%)	**0.85** (0.60 to 1.21)	**0.82** (0.58 to 1.15)
3	297	78 (26%)	**0.78** (0.56 to 1.09)	**0.75** (0.54 to 1.05)
4	52	12 (23%)	**0.69** (0.39 to 1.21)	**0.63** (0.35 to 1.13)
5 (highest level)	199	41 (21%)	**0.61** (0.41 to 0.90)	**0.60** (0.40 to 0.88)
			$P_{trend} = 0.01$	$P_{trend} = 0.01$
Current smoker				
No	702	172 (25%)	**1** (baseline)	
Yes	154	52 (34%)	**1.38** (1.07 to 1.78)	
BMI group (kg/m^2)				
<20	42	7 (17%)	**0.67 (0.33 to 1.35)**	
20-24.99	435	108 (25%)	**1** (baseline)	
25-29.99	230	60 (26%)	**1.05** (0.80 to 1.38)	
30-34.99	99	29 (29%)	**1.18** (0.83 to 1.67)	
≥35	44	18 (41%)	**1.65** (1.11 to 2.44)	
			$P_{trend} = 0.01$	
Reported extent to which stress has affected life				
None	208	43 (21%)	**1** (baseline)	**1** (baseline)
Slightly	333	88 (26%)	**1.28** (0.93 to 1.76)	**1.42** (1.02 to 1.98)
Moderately	171	50 (29%)	**1.41** (0.99 to 2.01)	**1.53** (1.06 to 2.21)
Quite a lot	122	35 (29%)	**1.39** (0.94 to 2.04)	**1.54** (1.05 to 2.28)
Extremely	24	8 (33%)	**1.61** (0.86 to 3.01)	**1.54** (0.83 to 2.86)
			$P_{trend} = 0.04$	$P_{trend} = 0.03$
Use of any hormonal contraceptive				
No	420	133 (32%)	1 (baseline)	1 (baseline)
Yes	413	83 (20%)	0.63 (0.50 to 0.81)	0.66 (0.52 to 0.84)